# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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**PCT**

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing *(day/month/year)* | 31 AUG 2005 |
| Applicant's or agent's file reference<br>STAN-353WO | **FOR FURTHER ACTION**<br>See paragraph 2 below |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/US05/09342 | 21 March 2005 (21.03.2005) | 25 March 2004 (25.03.2004) |

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/68; C12N 15/00; C07K 5/00 and US Cl.: 435/6, 69.1; 530/350

Applicant

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1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|---|---|
| Name and mailing address of the ISA/ US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230 | Authorized officer<br>Young J. Kim<br>Telephone No. (571) 272-1600 |

YOUNG J. KIM
PATENT EXAMINER

Form PCT/ISA/237 (cover sheet) (January 2004)

| WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY | International application No. PCT/US05/09242 |
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**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/09342

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**Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|---|---|---|
| Novelty (N) | Claims NONE | YES |
| | Claims 1-10 | NO |
| Inventive step (IS) | Claims NONE | YES |
| | Claims 1-10 | NO |
| Industrial applicability (IA) | Claims 1-10 | YES |
| | Claims NONE | NO |

2. Citations and explanations:

Please See Continuation Sheet

| WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY | International application No. PCT/US05/23342 |
|---|---|

**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 3 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim is indefinite for the following reason(s):

Claim 3 is dependent on claim 2. Claim 2 is drawn to a method of synthesizing biological macromolecules, wherein the method comprises translation of mRNA to produce polypeptides. Claim 3, however, is drawn to a method of synthesizing biological macromolecules, wherein the method comprises transcription of mRNA from DNA template. Claim 3 cannot further limit the parent claim 2 because the process defined in claim 2, that is, the process of translation occurs subsequent to transcription (process of claim 3). For the purpose of search and examination the claim is assumed to be dependent on claim 1.

**Supplemental Box**
**In case the space in any of the preceding boxes is not sufficient.**

**V. 2. Citations and Explanations:**
Claims 1 and 7-10 lack novelty under PCT Article 33(2) as being anticipated by Schmidt et al. (U.S. Patent No. 6,664,078 B1, issued December 16, 2003).

Schmidt et al. disclose a method of producing plasmid DNA (thus macromolecule) in the presence of Pluronic® (column 8, lines 43-44). The term, "*in vitro*," is accepted in the art as being "in test tube." While the instant description appears to be drawn to synthesis in a "cell-free" environment, such limitation is not explicit in the claims so as to preclude methods involving cell culturing in plates.

Schmidt et al. disclose a reaction mixture comprising an antifoam agent, Pluronic® (column 7, lines 29-30).
While Schmidt et al. are not explicit in their disclosure with regard to the actual concentration of the antifoam agent employed, said antifoam agent is employed in the isolation of macromolecules, and therefore, are assumed to meet the requisite concentration.
With regard to the intended use limitation, "[a] reaction mixture *for synthesis of biological macromolecules*," the intended use limitation is not given patentable weight so long as the prior art discloses the actual composition of the mixture, in this case, an antifoam reagent.

Therefore, Schmidt et al. anticipate the invention as claimed.

Claims 1, 3, and 7-10 lack novelty under PCT Article 33(2) as being anticipated by Marotta et al. (U.S. Patent No. 5,547,841, issued August 20, 1996).
Marotta et al. disclose a method of preparing RNA (which includes mRNAs), said method employing an antifoam reagent (column 9, lines 12-17).

Hence, Marotta et al. would also disclose a reaction mixture comprising an antifoam agent (column 9, lines 12-17).
While Marotta et al. are not explicit in their disclosure with regard to the actual concentration of the antifoam agent employed, said antifoam agent is employed in the production of RNA, and therefore, are assumed to meet the requisite concentration.
With regard to the intended use limitation, "[a] reaction mixture *for synthesis of biological macromolecules*," the intended use limitation is not given patentable weight so long as the prior art discloses the actual composition of the mixture, in this case, an antifoam reagent.

Therefore, Marotta et al. anticipate the invention as claimed.

Claims 1, 2, and 4-10 lack novelty under PCT Article 33(2) as being anticipated by Wight et al. (U.S. Patent No. 5,223,412, issued June 29, 1993).

Wight et al. disclose a method of producing protein in a cell-free system (column 5, line 62), wherein the method involves the use of an antifoam agent (column 6, line 8).

The term, "*in vitro*," is accepted in the art as being "in test tube." While the instant description appears to be drawn to synthesis in a "cell-free" environment, such limitation is not explicit in the claims so as to preclude methods involving cell culturing in plates.

Wight et al. disclose a reaction mixture comprising an antifoam agent, column 6, line 8).

**Supplemental Box**
**In case the space in any of the preceding boxes is not sufficient.**

While Wight et al. are not explicit in their disclosure with regard to the actual concentration of the antifoam agent employed, said antifoam agent is employed in the production of macromolecules, and therefore, are assumed to meet the requisite concentration. With regard to the intended use limitation, "[a] reaction mixture *for synthesis of biological macromolecules*," the intended use limitation is not given patentable weight so long as the prior art discloses the actual composition of the mixture, in this case, an antifoam reagent.

Therefore, Wight et al. anticipate the invention as claimed.

Claims 1-10 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry, especially in large-scale protein production.